Complete Summary

GUIDELINE TITLE

Age-related macular degeneration. Limited revision.

BIBLIOGRAPHIC SOURCE(S)

Retina Panel, Preferred Practice Patterns Committee. Age-related macular degeneration. San Francisco (CA): American Academy of Ophthalmology (AAO); 2005. 30 p. [107 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American Academy of Ophthalmology Retina Panel, Preferred Practice Patterns Committee. Age-related macular degeneration. San Francisco (CA): American Academy of Ophthalmology (AAO); 2003. 29 p.

All Preferred Practice Patterns are reviewed by their parent panel annually or earlier if developments warrant and updated accordingly. To ensure that all Preferred Practice Patterns are current, each is valid for 5 years from the "approved by" date unless superseded by a revision.

* * REGULATORY ALERT * *

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On April 7, 2006, Pfizer Pharmaceuticals notified healthcare professionals of important changes in the approved product labeling for Macugen (pegaptanib sodium injection), including changes to the CONTRAINDICATIONS, PRECAUTIONS, ADVERSE EVENTS Post-Marketing, and DOSAGE and ADMINISTRATION sections. Rare reports of anaphylaxis/anaphylactoid reactions, including angioedema following the administration of Macugen along with various medications administered as part of the injection preparation, were described. Macugen is indicated for the treatment of neovascular (wet) age-related macular degeneration, and is administered once every six weeks by intravitreous injection. Healthcare professionals should evaluate the patient's medical history for hypersensitivity reactions to Macugen prior to using this product. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Age-related macular degeneration

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Ophthalmology

INTENDED USERS

Health Plans
Physicians

GUIDELINE OBJECTIVE(S)

To minimize loss of vision and to maximize the vision-related quality of life related to age-related macular degeneration (AMD), by addressing the following goals:

- Identify patients at risk of visual loss related to age-related macular degeneration
- Educate patients and their families about the disease, risk factors, and preventive measures
- Minimize visual loss and functional impairment in these patients through appropriate detection, treatment, and follow-up examinations
- Help patients identify sources for visual rehabilitation

TARGET POPULATION

Persons typically age 50 years or older, with or without visual symptoms

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. History, including history of symptoms, medications and nutritional supplements, medical and ocular history, family history (especially of age-related macular degeneration [AMD]), social history (especially smoking)
2. Stereo biomicroscopic examination of the macula
3. Diagnostic tests, including fluorescein angiography and/or fundus photography when indicated.

Note: Indocyanine green video-angiography (ICG) and optical coherence tomography (OCT) were discussed but not specifically recommended.

Treatment/Management

1. Observation with no medical or surgical therapies
2. Antioxidant vitamin and mineral supplements
3. Thermal laser photocoagulation surgery
4. Photodynamic therapy (PDT) with verteporfin
5. Pegaptanib sodium intravitreal injection
6. Follow-up after treatment for neovascular AMD
7. Fundus photography and fluorescein angiograms, when indicated
8. Patient and family education
9. Referral to vision rehabilitation and social services

MAJOR OUTCOMES CONSIDERED

- Incidence of severe vision loss and functional impairment due to age-related macular degeneration
- Risks, benefits, and complications of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

In the process of revising this document, a detailed literature search of articles in the English language was conducted on the subject of age-related macular degeneration for the years 1997 to 2002.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Ratings of Strength of Evidence

- Level I includes evidence obtained from at least one properly conducted, well-designed randomized, controlled trial. It could include meta-analyses of randomized controlled trials.
- Level II includes evidence obtained from the following:
    - Well-designed controlled trials without randomization
    - Well-designed cohort or case-control analytic studies, preferably from more than one center
    - Multiple-time series with or without the intervention
- Level III includes evidence obtained from one of the following:
    - Descriptive studies
    - Case reports
    - Reports of expert committees/organization
    - Expert opinion (e.g., Preferred Practice Pattern panel consensus)

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The results of a literature search on the subject of age-related macular degeneration were reviewed by the Retina Panel and used to prepare the recommendations, which they rated in two ways. The panel first rated each recommendation according to its importance to the care process. This "importance to the care process" rating represents care that the panel thought would improve the quality of the patient's care in a meaningful way. The panel also rated each recommendation on the strength of the evidence in the available literature to support the recommendation made.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Ratings of Importance to the Care Process

Level A, most important
Level B, moderately important
Level C, relevant but not critical

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

These guidelines were reviewed by Council and approved by the Board of Trustees of the American Academy of Ophthalmology (September 2005).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Ratings of importance to the care process (A-C) and ratings of strength of evidence (I-III) are defined at the end of the "Major Recommendations" field.

Diagnosis

The initial evaluation of a patient with signs and symptoms suggestive of age-related macular degeneration (AMD) includes all features of the comprehensive adult medical eye evaluation, with particular attention to those aspects relevant to AMD.

History

An initial history should consider the following elements:

- Symptoms [A:II]
  - Metamorphopsia
  - Decreased vision
- Medications and nutritional supplements [B:III]
- Medical history [B:II]
- Ocular history [B:III]
- Family history, especially family history of AMD [B:II]
- Social history, especially smoking [B:II]

Examination

- Stereo biomicroscopic examination of the macula [A:III]

Binocular slit-lamp biomicroscopy of the ocular fundus is often necessary to detect subtle clinical clues of choroidal neovascularization (CNV). These include small areas of hemorrhage, hard exudates, subretinal fluid, or pigment epithelial elevation.

Diagnostic Tests

Fluorescein Angiography

Intravenous fundus fluorescein angiography in the clinical setting of AMD is indicated [A:I] when the patient complains of new metamorphopsia or has unexplained blurred vision, and/or when clinical examination reveals elevation of the retinal pigment epithelium (RPE) or retina, subretinal blood, hard exudates, or subretinal fibrosis and in the following situations:

- To detect the presence of and determine the extent, type, size, and location of CNV and to calculate the percentage of the lesion composed of or consisting of classic CNV. If laser photocoagulation surgery or verteporfin photodynamic therapy (PDT) is being considered, the angiogram is also used as a guide to direct treatment.
- To detect persistent or recurrent CNV following treatment
- To assist in determining the cause of visual loss that is not explained by the clinical examination.

If CNV is suspected on the basis of new symptoms or ocular findings, fluorescein angiography should be performed and interpreted expeditiously by an individual experienced in managing patients with neovascular AMD. [A:I]

If fluorescein angiography is to be performed, the physician must be aware of potential risks associated with this procedure; severe medical complications may occur, including death (approximately 1 in 200,000 patients). Each angiographic facility should have in place a care plan or an emergency plan and a clear protocol to minimize the risks and to manage any complications. [A:III]

Fundus Photography

Stereoscopic color fundus photographs are usually obtained when angiography is performed, because they are useful in finding landmarks, evaluating serous detachments of the sensory retina and RPE, and determining the etiology of blocked fluorescence or late leakage of undetermined source. Stereo photographs may also be used as a baseline for selected patients with advanced non-neovascular AMD and for follow-up of treated patients.

Ancillary Tests

Indocyanine green video-angiography is a technique that allows viewing of the choroidal circulation. The value of this test in evaluating and treating AMD remains unknown. It may prove useful in evaluating certain types of AMD, such as pigment epithelial detachment, poorly defined CNV, and lesions such as retinal angiomatous proliferation. Optical coherence tomography (OCT) may be helpful in

determining the presence of subretinal fluid and in documenting the degree of retinal thickening, but the value of this test in evaluating and treating AMD remains unknown. Optical coherence tomography probably provides information that is complementary to fluorescein angiography.

Treatment

Assessment and treatment plans for different categories of AMD are listed in the table below.

Recommended Treatment	Diagnoses Eligible for Treatment	Follow-up Recommendations
Observation with no medical or surgical therapies [A:I]	No clinical signs of AMD (Age-Related Eye Disease Study [AREDS] category 1) Early AMD (AREDS category 2) Advanced AMD with bilateral subfoveal geographic atrophy or disciform scars	As recommended in the Comprehensive Adult Medical Eye Evaluation Preferred Practice Pattern (PPP) [A:III] No fundus photos or fluorescein angiography unless symptomatic [A:I]
Antioxidant vitamin and mineral supplements as recommended in the AREDS reports [A:I]	Intermediate AMD (AREDS category 3) Advanced AMD in one eye (AREDS category 4)	Monitoring of monocular near vision (reading/Amsler grid) [A:III] Return exam at 6 to 24 months if asymptomatic or prompt exam for new symptoms suggestive of CNV [A:III] Fundus photography as appropriate Fluorescein angiography if there is evidence of edema or other signs and symptoms of CNV
Thermal laser photocoagulation surgery as recommended in the Macular Photocoagulation Study (MPS) reports [A:I]	Extrafoveal classic CNV, new or recurrent Juxtafoveal classic CNV May be considered, although rarely used, for new or recurrent subfoveal CNV if the lesion is less than 2 MPS disc areas and the vision is 20/125 or	Return exam with fluorescein angiography approximately 2 to 4 weeks after treatment, and then at 4 to 6 weeks and thereafter depending on the clinical and angiographic findings [A:III] Retreatments as indicated

Recommended Treatment	Diagnoses Eligible for Treatment	Follow-up Recommendations
	worse, especially if PDT is contraindicated or not available May be considered for juxtapapillary CNV	Monitoring of monocular near vision (reading/Amsler grid) [A:III]
PDT with verteporfin as recommended in the Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) and Verteporfin in Photodynamic Therapy (VIP) reports [A:I]	Subfoveal CNV, new or recurrent, where the classic component is >50% of the lesion and the entire lesion is ≤5400 microns in greatest linear diameter Occult CNV may be considered for PDT with vision <20/50 or if the CNV is <4 MPS disc areas in size when the vision is >20/50.	Return exam with fluorescein angiography every 3 months until stable, with retreatments as indicated [A:III] Monitoring of monocular near vision (reading/Amsler grid) [A:III]
Pegaptanib sodium intravitreal injection as recommended in pegaptanib sodium literature [A:I]	Subfoveal CNV, new or recurrent, for predominantly classic lesions ≤12 MPS disc areas in size Minimally classic, or occult with no classic lesions where the entire lesion is ≤12 disc areas in size, subretinal hemorrhage associated with CNV comprises ≤50% of lesion, and/or there is lipid present, and/or the patient has lost 15 or more letters of visual acuity during the previous 12 weeks	Patients should be instructed to report any symptoms suggestive of endophthalmitis without delay, including eye pain or increased discomfort, worsening eye redness, blurred or decreased vision, increased sensitivity to light, or increased number of floaters [A:III] Return exam with retreatments every 6 weeks as Indicated [A:III] Monitoring of monocular near vision (reading/Amsler grid) [A:III]

Note: If patients treated with thermal laser photocoagulation surgery, verteporfin PDT, or pegaptanib sodium injection notice visual loss or change prior to the next scheduled visit, return evaluation that may include angiography is recommended. [A:III]

The risks, benefits, and complications of the treatment should be discussed with the patient and informed consent obtained (see Counseling/Referral). [A:III]

Patients with CNV that meets the MPS criteria or with subfoveal CNV that meets TAP or VIP criteria for a predominantly classic lesion or an occult lesion with no classic CNV should be treated within 1 week after fluorescein angiography. [A:I]

Complications of Treatment

Patients who smoke cigarettes or who stopped within the last year should be advised to avoid taking beta-carotene. [A:III]

Introduction or enlargement of a pre-existing scotoma, with or without visual acuity loss, is not a complication of thermal laser photocoagulation surgery; it is an anticipated side effect of the treatment. Similarly, recurrence or persistence of CNV, or the development of new CNV and further visual deterioration after adequate thermal laser surgery, is usually a result of the disease process and is not a complication. These realities must be emphasized to the patient and family prior to treatment. [A:III]

Follow-up

A history and examination are the recommended elements of the follow-up visits. Recommended follow-up intervals are listed in the above table.

History

The follow-up history should take into account the following:

- Symptoms, including decreased vision and metamorphopsia [A:II]
- Changes in medications and nutritional supplements [B:III]
- Changes in medical and ocular history [B:III]
- Changes in social history (smoking) [B:II]

Examination

The examination on the follow-up visit should include the following:

- Visual acuity [A:III]
- Stereo biomicroscopic examination of the fundus [A:III]

Diagnostic tests used in the follow-up examination are identical to those listed under "Diagnosis," and the treatment plan is identical to the one described under "Treatment."

Follow-up after Treatment for Neovascular AMD

In addition to the above recommendations, patients who have been treated with thermal laser photocoagulation surgery, verteporfin PDT, or pegaptanib sodium injection should be examined at regular intervals by means of biomicroscopy of the fundus. [A:III] Fundus photography [A:III] and fluorescein angiography [A:I] should be employed when indicated.

A follow-up examination and fluorescein angiography should be performed approximately 2 to 4 weeks after initial thermal laser photocoagulation surgery to confirm that the CNV has been obliterated. [A:I] Subsequent examinations and fluorescein angiography should be performed at approximately 4 to 6 weeks and thereafter depending on the clinical findings and the judgment of the treating physician. [A:I] Subsequent fluorescein angiograms can be used to complement the clinical examination because persistent or recurrent CNV is common and may

be clinically subtle or undetectable. Treated patients who report new symptoms may need to be re-examined promptly and before their next scheduled follow-up visit.

Following verteporfin PDT for subfoveal CNV, follow-up examinations and fluorescein angiograms may be recommended at least every 3 months until stable, with retreatments as indicated. [A:III]

Following pegaptanib sodium injection, follow-up examinations should occur approximately 6 weeks following the treatment. [A:III] Subsequent examinations, OCT, and fluorescein angiography should be performed as indicated depending on the clinical findings and the judgment of the treating ophthalmologist. [A:III] Treated patients should be instructed to report symptoms of endophthalmitis and should be re-examined promptly. [A:III]

Fellow Eye

For patients with unilateral disease, the fellow eye without CNV remains at high risk of developing advanced AMD. The risk can be significantly lowered over a 5-year period by taking the AREDS supplements. Patients should be instructed to monitor their vision and to return to the ophthalmologist periodically, even in the absence of symptoms, but promptly after the onset of any new or significant visual symptoms. [A:III]

Provider

Treatment of CNV is difficult, and referral to an ophthalmologist with special training or experience in managing this condition is appropriate.

Ancillary clinical personal should be aware that patients with the onset of new symptoms suggestive of AMD (e.g., new visual loss, metamorphosia, or scotoma) should be examined promptly. [A:III]

Counseling/Referral

All patients with AMD should be educated about the prognosis of the disease and the potential value of treatment as appropriate for their ocular and functional status. [A:III]

Patients with early AMD who may develop the intermediate or more severe stages of AMD should be encouraged to have regular dilated eye exams for the early detection of the intermediate stage of AMD. [A:III]

Patients with intermediate AMD who are at increased risk of visual loss or of progression to advanced AMD should be educated about methods of detecting new symptoms of CNV and about the need for prompt notification to an ophthalmologist who can confirm if the new symptoms are from CNV and who can begin treatment if indicated. [A:III]

Patients with CNV for whom treatment may be indicated, based on the MPS, TAP, and VIP, and VISION trials, should be counseled about the effects of treatment, [A:III] some of which are as follows:

- Treatment will reduce but not eliminate the risk of severe visual loss.
- Thermal laser surgery will produce permanent scotomas. The location, size, and anticipated effect of the scotoma on central visual function (e.g., reading vision) should be explained.
- Verteporfin PDT and pegaptanib sodium injection will reduce the risk of moderate and severe visual loss, but most patients will still lose some vision over 2 years, and improvement in visual acuity is unusual. The dosing regimen upon which efficacy was demonstrated in the clinical trials included PDT administration every 3 months if evidence of leakage on fluorescein angiography, and pegaptanib sodium injection every 6 weeks.
- There is a high risk of CNV persistence or recurrence after thermal laser surgery that could require additional laser surgery. This risk is greatest during the first year after initial treatment.
- Multiple fluorescein angiograms are necessary for appropriate follow-up after thermal laser surgery, verteporfin PDT, or pegaptanib sodium injection.

Patients with reduced visual function should be referred for vision rehabilitation and social services. [A:III]

Definitions:

Ratings of Importance to Care Process

Level A, most important
Level B, moderately important
Level C, relevant but not critical

Ratings of Strength of Evidence

- Level I includes evidence obtained from at least one properly conducted, well-designed randomized, controlled trial. It could include meta-analyses of randomized controlled trials.
- Level II includes evidence obtained from the following:
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- Level III includes evidence obtained from one of the following:
    - Descriptive studies
    - Case reports
    - Reports of expert committees/organization
    - Expert opinion (e.g., Preferred Practice Pattern panel consensus)

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for most recommendations (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved vision or minimized visual loss and functional impairment related to age-related macular degeneration (AMD)

POTENTIAL HARMS

A brief list of complications is given below. Refer to the original guideline document for a more detailed discussion.

Fluorescein Angiography Testing

- Severe medical complications may occur, including death (approximately 1 in 200,000 patients)

Supplements of High-dose Antioxidants and Zinc

- Beta-carotene
    - Increased yellowing of the skin
    - Increased risk of developing lung cancer in current smokers or former smokers who stopped within the last year
- Zinc
    - Increased risk of hospitalizations for genitourinary causes (prostate hypertrophy in men)

Thermal Laser Photocoagulation Surgery

- Severe vision loss following treatment, which may be permanent
- Rupture of Bruch's membrane with subretinal or vitreous hemorrhage
- Retinal pigment epithelium (RPE) tears
- Treatment of the fovea in juxtafoveal neovascularization

Photodynamic Therapy (PDT)

- Severe vision loss within 1 week following treatment in 1 to 4%, which may be permanent
- Infusion site extravasation requiring coverage of the infiltrated area for 5 days or until it is normal
- Idiosyncratic back pain during infusion of drug in 1% to 2%
- Photosensitivity reaction (can be avoided by avoiding direct sunlight)

Pegaptanib Sodium Injection

- Endophthalmitis (1.3% of treated cases during first year of treatment)
- Traumatic injury to the lens (0.6% of treated cases during first year of treatment)
- Retinal detachment (0.7% of treated cases during first year of treatment)

Other adverse events reported more frequently in the group treated with pegaptanib sodium injection compared with the control group were eye pain, vitreous floaters, punctate keratitis, vitreous opacities, cataract, anterior chamber inflammation, visual disturbance, eye discharge, and corneal edema.

CONTRAINDICATIONS

CONTRAINDICATIONS

The use of verteporfin photodynamic therapy (PDT) is contraindicated in patients with porphyria or a known allergy or sensitivity to the drug, and careful consideration should be given to patients with liver dysfunction, and patients who are pregnant, breastfeeding, or of pediatric age because these patients were not studied in published reports.

QUALIFYING STATEMENTS

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- Preferred Practice Patterns provide guidance for the pattern of practice, not for the care of a particular individual. While they should generally meet the needs of most patients, they cannot possibly best meet the needs of all patients. Adherence to these Preferred Practice Patterns will not ensure a successful outcome in every situation. These practice patterns should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the best results. It may be necessary to approach different patients' needs in different ways. The physician must make the ultimate judgment about the propriety of the care of a particular patient in light of all of the circumstances presented by that patient. The American Academy of Ophthalmology is available to assist members in resolving ethical dilemmas that arise in the course of ophthalmic practice.
- Preferred Practice Patterns are not medical standards to be adhered to in all individual situations. The Academy specifically disclaims any and all liability for injury or other damages of any kind, from negligence or otherwise, for any and all claims that may arise out of the use of any recommendations or other information contained herein.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Sep (revised 2005)

GUIDELINE DEVELOPER(S)

American Academy of Ophthalmology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Ophthalmology

GUIDELINE COMMITTEE

Retina Panel; Preferred Practice Patterns Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The following authors have received compensation within the past 3 years up to and including August 2005 for consulting services regarding the equipment, process, or product presented or competing equipment, process, or product presented:

Tom S. Chang, MD: Bausch and Lomb, Genentech, iScience, Novartis, Visioncare -- Ad hoc consulting fees.

H. Culver Boldt, MD: Alcon -- Contribution to travel funds.

Joan W. Miller, MD: Alnylam Pharmaceuticals, Bausch and Lomb, Genentech -- Ad hoc consulting fees. Additional Disclosure: The Massachusetts Eye and Ear Infirmary has an ownership in three U.S. patents directed to the use of verteporfin. In addition, the Massachusetts Eye and Ear Infirmary has an ownership interest in certain patent applications directed to the selective destruction of subretinal choroidal neovasculature for the treatment of macular degeneration and other disorders. Should the Massachusetts Eye and Ear Infirmary receive royalties or other financial remuneration as a result of these patents and patent applications, Dr. Miller would receive a share of the same in accordance with the Massachusetts Eye and Ear Infirmary's institutional Patent Policy and Procedures, which includes royalty-sharing provisions.

Marco A. Zarbin, MD, PhD: Johnson & Johnson -- Contract payments for research performed. Genentech, Novartis -- Ad hoc consulting fees.

Other authors have no financial interest in the equipment, process, or product presented or competing equipment, process, or product presented.

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GUIDELINE AVAILABILITY

Electronic copies: Available from the American Academy of Ophthalmology (AAO) Web site.

Print copies: Available from American Academy of Ophthalmology, P.O. Box 7424, San Francisco, CA 94120-7424; telephone, (415) 561-8540.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on February 20, 1999. The information was verified by the guideline developer on April 23, 1999. This summary was updated on January 08, 2002. The updated information was verified by the guideline developer as of February 19, 2002. This summary was updated again on April 30, 2004. The information was verified by the guideline developer May 20, 2004. This NGC summary was updated by ECRI on January 5, 2006. The updated information was verified by the guideline developer on February 9, 2006. This summary was updated by ECRI on April 12, 2006 following the U.S. Food and Drug Administration (FDA) advisory on Macugen (pegaptanib sodium injection).

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